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Mini Review

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Review of Pharmacological Roles of Vinegar-Baked Radix Bupleuri

Abstract

The efficacy of Bupleuri Radix is enhanced with vinegar enhancing the water solubility of active substances in herbs with its detoxifying effects to increase the pharmacological activities and proved to outperform raw Bupleuri Radixin treating liver diseases with science-based evidence. However, the differences like if the best efficacy can occur when the adjuvant is not vinegar, whether or not Bupleuri Radix can damage Yin, and Bupleurum chinense DC. or Bupleurum scorzonerifolium Willd should be considered for clinical use need more research works in the future.

Keywords: vinegar; Bupleuri Radix; Saikosaponin

Introduction

With the news that Chinese herbs have been accepted to use by the Olympic athletes, traditional Chinese medicine (TCM) herbs are gaining the attention and popularity and are recognized as the part of the healthcare system in the West like acupuncture, even though they are at present still viewed as the complementary and alternative healthcare tools. Pattern derived from the Yin-Yang theory is surely the key concept of the TCM for the successful treatment out comes. The dried root of Bupleurum Chinense DC, Bupleuri Radix (柴胡, Chaihu in Chinese), is one of the attractive TCM herbs in the Chinese communities for years and has been widely selected to treat the liver-related symptoms based on the TCM pattern identifications, such as dizziness, fever, jaundice, hepatitis, nephritis [1]. TCM herbs can possess different therapeutic effects before and after processing, which is a pharmaceutical technique to transform raw herbs into decoction pieces for specific purposes at different treatment stages. The current adjuvants often used are honey, vinegar, wine, and brine to reduce the toxicity of raw herbs to enhance the efficacy [2].

This review tries to present the evidence-based studies of vinegar-baked Bupleuri Radix (VBRB) to understand the mechanisms of pharmacological effects.

References Reviewed

Vinegar-baked Radix Bupleuri (VBRB) is often used in the TCM to liver diseases. However, the results of Chemical and biological comparison of raw and vinegar-baked Radix Bupleuri show both raw and processed Radix Bupleuri possess liver protective effects against CCl4 induced liver injury, and the vinegar-baked Radix Bupleuri outperforms raw Radix Bupleuri [3]. Doses of vinegar seem to play the key role to affecting the efficacy. In the research Vinegar amount in the process affected the components of vinegar-baked Radix Bupleuri and its hepatoprotective effect [4], the hepatoprotective effects of vinegar-baked Radix Bupleuri with different amount of vinegar (1:5, 2:5, 3:5) on liver hurt rats and the change of constituents analyzed by ultra-performance liquid chromatography tandem mass spectrometry (UPLC-MS/MS) suggest that vinegar amount can affect the pharmacological effect of VBRB and saikosaponin b2 significantly.

The chemical mechanism of the processing of vinegar-baked Radix Bupleuri is explored with an ultra-high performance liquid chromatography with quadruple time-of-flight mass spectrometry coupled with multivariate statistical analysis to compare the difference between raw and vinegar-baked Bupleuri Radix. A total of 49 peaks chemical compounds were identified, while 50 peaks in both raw and processed Bupleuri Radix were detected with the potential markers of raw and vinegar-baked Bupleuri Radix like Saikosaponin a, Saikosaponin d, Saikosaponin b3, Saikosaponin e, Saikosaponin c, Saikosaponin b2, Saikosaponin b1, 4”-O-acetyl-Saikosaponind, hyperoside and 3’, 4’-dimethoxy quercetin. In addition, the changes of chemical profiling was predicted to be closely related to the underlying hepatoprotective mechanism of Bupleuri Radix [5].

Saikosaponins are the main active ingredient of Bupleuri Radix and attract much more attention in the present evidenced-based studies. Heat works together with acetic acid in vinegar to promote complex chemical reactions like salification, pyrolysis, esterification, and hydrolysis. The 13,28-epoxy bridges transformed into a heteroanulare diene structure to convert Saikosaponins a, c, and d into Saikosaponins b1 and b2, in which Saikosaponins a and d possess anti-inflammatory activities and Saikosaponin b, hepatoprotective [6].

For understanding the pharmacokinetic characteristics of
Saikosaponin a (SSa), which is the most abundant Saikosaponin in Bupleuri Radix and possesses pharmacological activities like anti-inflammatory, antitumor, antiviral, immunoregulatory, neuromodulatory, and hepatoprotective activities, the results of Effects of Animal Strain, Dose, and Cotreatment with Saikosaponin b2 (SSb2) on the pharmacokinetics of Saikosaponin a in Rats show the pharmacodynamic mechanism of Bupleuri Radix can be explained with the absorption of SSa in Wistar rats which is superior to that in Sprague Dawley rats in the peak concentration (C_max) and the area under the concentration–time curve (AUC0–t). Different doses of SSa in Wistar rats in the pharmacokinetic studies reveal that the systemic exposure of SSa can increase with dose disproportionately, which indicates that SSa possesses non-dose-proportional pharmacokinetics. In addition, SSb2 is a characteristic component of vinegar-baked Radix Bupleuri that can inhibit the absorption of SSa in rats [7] and increase colchicine efflux in HEK293 cells by increasing Mrp1 activity to enhance Mrp2 function and increased cisplatin efflux in BRL3A cells [8]. In the comparative pharmacokinetic study in depression rats after oral administration of extracts of raw and vinegar-baked Bupleuri Radix, comparative pharmacokinetic profiles of the eight Saikosaponins (SSa, SSb1, SSb2, SSb3, SSb4, SSC, SSD, and SSf) show AUC0–t and C_max were significantly different after oral administration of extracts of raw and vinegar-baked Bupleuri Radix [9].

It is claimed the effects of pharmacological activity of vinegar-baked Radix Bupleuri depend on the increased drug accumulation in the liver. In Saikosaponins A, C and D enhance liver-targeting effects of anticancer drugs by modulating drug transporters, the effects of the main components Saikosaponin A, C, and D on drug transporters are presented with the evidence that Saikosaponins affects drug transporters with a transporter expression amount depending manner to induce liver targeting effect [10].

Vinegar-baked Radix Bupleuri may be associated with drug transporters to potentiate the activity of anticancer drugs in the liver through increasing their hepatic distribution. It is reported in Clerosterol from vinegar-baked radix bupleuri modifies drug transport that the combination of vinegar-baked Radix Bupleuri (VBRB) and traditional chemotherapy may modify drug transport in treating liver cancer [11].

The result of the study on the effect of clerosterol, which may be an active constituent of VBRB to work against cancer multidrug resistance by inhibiting Pgp activity with its marginal effects on Mrp2 and Mrp1 activity in Mrp2- and Mrp1-overexpressing HEK293 cells reveals clerosterol can increase Mrp2 gene expression to decrease cisplatin uptake in BRL cells and decrease the uptake of colchicine in HEK 293 cells through increasing Pgp and Mrp1 activity. In addition, mRNA and OCT2 protein increase to enhance OCT2 activity in HEK293-Pgp cells. On the other hand, vinegar-baked Radix Bupleuri is proved to effectively enhance the liver-targeting efficiency of 10-Hydroxycamptothecin (HCPT) loaded polymeric micelles after oral coadministration with the data that low and medium dose of BC1 outperform the high dose in liver-targeting effects [12].

Discussion

Traditionally, vinegar is used as a processing tool in the TCM for its physiological effects with ligustrazine, esters, organic acids, aldehydes, alcohols, phenols, and flavonoids. Different from other adjuvants commonly used like honey, wine, brine, and oil, vinegar can increase thewatar solubility of active substances in herbs with its detoxifying effects to increase the pharmacological activities. The scientific evidence shows vinegar-baked Bupleuri Radix has a stronger effect than unprocessed Bupleuri Radix in treating liver diseases through soothing liver [6], which suggests that Bupleuri Radix must be baked with vinegar to reach the goal of treating liver diseases, including liver cancer. However, it deserves attention when the Saikosaponins like Saikosaponin b bearing hepatoprotective effect can be decreased or disappear if they are cooked.

What needs attention for understanding the efficacy of vinegar-baked Radix Bupleuri is that patterns are often ignored and not included in the research verifying and exploring the efficacy of vinegar-baked Radix Bupleuri. In other words, most studies focus on the chemical ingredients and pharmacological activity. It is noted that whether or not the use of vinegar-baked Bupleuri Radix can reach the goal in practice rely mainly on the accurate patterns.

In addition, it has been a myth in the TCM classics for years that Radix Bupleuri can deprive human body of Yin, which serves as the fundamental material to provide Zang-Fu organs with energy to work. The present scientific evidence has not proved and explained what kind of Yin from the scientific perspective Radix Bupleuri can damage.

Radix Bupleuri is derived from the dried roots of either Bupleurum chinense DC. (Pei-north Chaihu, 北柴胡) or Bupleurum scorzonerifolium Wild. (Nan–south ChaiHu, 南柴胡). However, it remains uncertain for years whether or not Bupleurum chinense DC in the most famous and frequently used preparations Da Chai Hu decoction and Xiao Chai Hu decoctionis the main ingredient. In theory, the major differences between Bupleurum scorzonerifolium and Wild Bupleurum chinense DC. Are the indication of Bupleurum chinense DC. is to disperse stagnated Liver qi while Bupleurum scorzonerifolium Wild is raising Yang Qi in the pattern of the Middle Jiao deficiency [1].

Conclusion

Various pharmacological effects of vinegar have been explored, but more research is needed to understand and solve the issues listed above for understanding more about the therapeutic effect of vinegar-processed herbal medicines. Furthermore, more research works are needed to understand the benefits of vinegar in the processing of either Bupleurum chinense DC. or Bupleurum scorzonerifolium Wild.
References


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